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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,239	10/18/2001	Rita De Santis	2818-64	6035

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[REDACTED] EXAMINER

QIAN, CELINE X

[REDACTED] ART UNIT      [REDACTED] PAPER NUMBER

1636

DATE MAILED: 04/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/981,239	DE SANTIS, RITA
	<b>Examiner</b>	<b>Art Unit</b>
	Celine X Qian	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 24 February 2003.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 32-35,39-43 and 46-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 32-35,39-43 and 46-49 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)           | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ .                                   |

### **DETAILED ACTION**

Claims 32-35, 39-43, 46-49 are pending in the application. Claims 36-38, 44 and 45 are cancelled.

This Office Action is in response to the Amendment filed on 2/24/03.

#### *Response to Amendment*

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

The objection to claim 48 has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 32-48 under 35 U.S.C.112 1<sup>st</sup> paragraph has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 32-47 under 35 U.S.C.112 2<sup>nd</sup> paragraph has been withdrawn in light of Applicants' amendment of the claims.

Claim 39 is rejected by 35 U.S.C.112 2<sup>nd</sup> paragraph for reasons discussed below.

Claims 32-35, 39, 42, 47-49 are rejected under 35 U.S.C.102 for reasons discussed below.

Claims 40, 41 and 43 and 46 are rejected under 35 U.S.C.103(a) for reasons discussed below.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of “wherein said peripheral blood monocellular cells are Epstein-Barr virus-immortalized B-lymphoblastoid cell lines” renders the claim indefinite because it is unclear what the claim encompasses. Claim 32 recites “collecting peripheral blood mononuclear cells from a subject,” however, it is unclear how to collect an EBV-transformed cell line from a subject because usually cell lines are generated *in vitro*.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-35, 39, 42, 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Shichijo et al (1996, Jpn. J. Cancer Res. Vol 87, pages 751-756).

Shichijo et al. disclose a method for generation of cells expressing cancer testis antigen MAGE, comprising the steps of collecting peripheral blood mononuclear cells from healthy volunteers and patients with adult T cell leukemia; activating said collected cells by PHA and IL-

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2, followed by incubation for an additional 8 days with PHA and IL-2 in the presence or absence of 5-aza-2'-deoxycytidine (DAC) (see page 751, bridging paragraph of col.1 and col.2, and col.2, 2<sup>nd</sup> paragraph). Shichijo et al. disclose that 4 Epstein-Barr virus transformed B cell lines are also treated with DAC. Shichijo et al. further disclose that T cells, B cells, monocytes and myeloid cells from healthy or leukemia patients expressing multiple cancer testis antigen MAGE1, 2, 3 and 6 following DAC treatment (see Table 1). Therefore, Shichijo et al. disclose the instantly claimed invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shichijo et al., in view of Hu et al (2000, Endocrinology, Vol 141, No.12, pages 4428-4435).

The teaching of Shichijo et al. is discussed above. Shichijo et al. further teach that demethylation of CpG in MAGE promoter up-regulate the accessibility of DNA to transcription factor to the promoter thereby induce MAGE gene expression (see 755, 2<sup>nd</sup> col., lines 1-6). However, Shichijo et al. do not teach further treating cells with histone deacetylase inhibitor.

Hu et al. teach that histone acetylation accompanies genomic imprinting of the insulin-like growth factor II receptor gene (Igf2r, see abstract). Hu et al. teach that treating cultured fibroblasts with histone deacetylase inhibitor Trichostatin A induces partial relaxation of genomic imprinting as well as decreased DNA methylation of both Igf2r promoters (Figure 4).

Hu et al. further teach that DNA demethylating agent DAC and histone deacetylase inhibitor have synergistic effect that lead to the loss of genomic imprinting (see page 4434, col1, paragraph 3-5).

It would have been obvious to one of ordinary skill of art to include the step of treating cells with a histone deacetylase inhibitor for the method of inducing cells expressing cancer testis antigen because of the combination teaching of Shichijo et al., who teach a method of generating cells expressing cancer testis antigen by using demethylating agents, and Hu et al., who teach histone deacetylase inhibitor act synergistically with demethylating agent in inducing gene expression. One of ordinary skill of art would have been motivated to do so to increase expression of cancer testis antigen in these cells. The level of skill in the art is high. Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation of success to generate cells expressing cancer testis antigen by using both demethylating agents and histone deacetylase inhibitor. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Claims 40, 41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shichijo et al., in view of Schultze et al. and McKearn et al.

The teaching of Shichijo et al. is discussed above. However, Shichijo et al. do not teach that the cells are activated by CD40, pokeweed mitogen or combination of pokeweed mitogen and IL-2 and PHA.

McKearn et al. teach that pokeweed mitogen is a mitogenic compound that can be used stimulate B cell (see page 7, 2<sup>nd</sup> paragraph).

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Schultz et al. teach that CD40 activated B cells is a highly efficient APC source (see abstract).

It would have been obvious to one of ordinary skill of art to activate the collected PBMC cells by CD40, PWM or combination of PWM, PHA and IL-2 because of combined teaching of Shichijo et al., McKearn et al. and Schultz et al. The ordinary artisan would have been motivated to do so because Schichijo et al. have taught a method of generating cells presenting MAGE by demethylating activated PBMC, and CD40, PWM are commonly used agents to stimulate B cells. The level of skills in the art is high. Absent evidence from the contrary, one of ordinary skill or art would have reasonable expectation to generate cells expressing cancer testis antigen as claimed. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*Anne-Marie Falk*  
ANNE-MARIE FALK, PH.D.  
PRIMARY EXAMINER

Celine Qian, Ph.D.

April 22, 2003